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Surgical and systemic management of endometrial cancer: an international survey

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Abstract

Purpose—To ascertain the spectrum of clinical management of endometrial carcinoma (EC) the largest international survey was conducted to evaluate and identify differences worldwide.

Methods—After validation of a 15-item questionnaire regarding surgical and adjuvant treatment of EC in Germany, an English-adapted questionnaire was put online and posted to all the major gynecological cancer Societies worldwide for further distribution commencing in 2010 and continued for 26 months.

Results—A total of 618 Institutions around the world participated: Central Europe (CE), Southern Europe (SE), Northern Europe (NE), Asia and USA/Canada/UK. Both a therapeutic and staging value was attributed to systematic pelvic and paraaortic lymph node dissection (LND) in CE (74.6 %) and in Asia (67.2 %), as opposed to USA/UK where LND was mainly for staging purposes (53.5 %; $p < 0.001$). LND was performed up to the renal veins in CE in 86.8 %, in Asia in 80.8 %, in USA/UK in 51.2 % and in SE in 45.1 % ($p < 0.001$) of cases. In advanced disease, centers from Asia were treated most with adjuvant chemotherapy alone (93.6 %), as opposed to centers in SE, CE and UK/USA that employed combination chemoradiotherapy in 90.9 % ($p < 0.001$) of cases. Paclitaxel/carboplatin was mostly used followed by doxorubicin/cisplatin (75 vs. 23.3 %; $p < 0.001$). In total, 94 % of all participants supported the concept of treating EC patients within appropriate clinical trials.

Conclusions—There is broad range in both the surgical and adjuvant treatment of EC across different countries. Large-scale multicenter prospective trials are warranted to establish consistent, evidence-based guidelines to optimize treatment worldwide.

Keywords

Endometrial cancer; Survey; Lymph node dissection; Toxicity; Chemotherapy

Introduction

Endometrial cancer (EC) is the most common women's malignancy worldwide [1]. The optimal management of EC remains one of the most contentiously debated issues in the gynecologic oncologic discipline, as evidenced by markedly disparate national and international guidelines. Even though surgery is the gold standard for the majority of newly diagnosed patients, unresolved questions remain as to the optimum extent of surgical radicality, the precise role of lymphadenectomy, the most appropriate adjuvant chemotherapeutic regime and the survival benefit of external beam radiotherapy [2–4]. In the relapsed setting there is even greater debate regarding the preferential therapeutic modalities.

In recent years, various trials have been designed in an attempt to address these questions. However, final conclusions and international agreement have been hampered by the varied surgical beliefs and practices, preferences for adjuvant therapies that have influenced trial development and sometimes compromising studies to ensure recruitment. These biases have resulted in the potential for distorted interpretation and application of the trial results into clinical practice [5–8].

The aim of this study was to identify physicians practice in an international setting, to ascertain choices in the surgical, chemo- and radio-therapeutic management of primary and relapsed EC.

Materials and methods

The present survey was initiated by the North-Eastern-German Society of Gynaecologic-Oncology (NOGGO). The survey commenced in April 2010 and finished in July 2012. The format employed was both online (www.noggo-endometrium.com) and a posted questionnaires forwarded to all major gynecological cancer Societies worldwide for further distribution. The survey was supported by the GCIG (Gynecologic Cancer Intergroup) and ENGOT (European Network of Gynecological Oncological Trial Groups) and developed from pilot surveys originally performed in 2003 and repeated on a larger scale in 2009 in all gynecological oncologic centers in Germany. The 15-itemed-questionnaire regarding surgical and adjuvant procedures of EC was validated in the German language. Following the successful outcome of these surveys [30] the English-adapted questionnaire was developed and distributed based on the current contentious questions regarding the treatment of endometrial cancer. Choice was given to answer the questionnaire anonymously.

The survey received official support from the major gynecological oncologic societies and study groups worldwide: the SGO, the EORTC, the JGOG, the KGOG, the ASGO, the SPS, the IGCS and the GCIG.

The focus of the 15-item questionnaire was on the surgical, chemotherapeutic and radio-therapeutic treatment of primary EC and questions were followed by multiple-choice answers. The entire questionnaire can be found in the supplement file of this article (Appendix 1).

Statistical analysis

For the description of all characteristics, frequency and percentages are reported. Associations between the hospital characteristics and other variables were evaluated using Chi²-test, Fisher's exact-test or Kendall tau-b where appropriate. All data were analyzed using IBM®-SPSS®-Statistics20 (SPSS Inc., Chicago, IL) and $p < 0.05$ was considered statistically significant.

Results

Between April 2010 and July 2012, 618 questionnaires from 24 countries across all 5 continents were completed and returned either online or via post to the NOGGO-

headquarters. Asia (Japan, Korea, Taiwan): 125 (20.2 %); Group Central Europe –CE– (Germany, Austria, Switzerland): 366 (59.2 %); Group Northern Europe –NE– (Belgium, Denmark, Finland, Norway, Sweden, Netherlands): 18 (3 %); Group Southern Europe–SE–: (Portugal, Spain, Greece, Italy, Poland, Israel, Turkey): 52 (8.4 %); Group Australia/New Zealand: 13 (2.1 %) and Group United states/United Kingdom/Canada: 44 (7.2 %).

The majority ($n = 410$; 66.3 %) of the participants were non-academic, while 207 (33.5 %) were from university hospitals. The majority of participants ($n = 580$; 93.9 %) supported enrollment of EC patients in national and international clinical trials. The number of cases managed annually in a center was used as a surrogate marker of the centers ‘expertise’. A total of 194 centers (31.4 %) treated 20 cases per year; 187 centers (30.3 %) 21–40 cases; 100 centers (16.2 %) 41–80 cases; 32 centers (5.2 %) 81–100 cases; 16 centers (2.6 %) 101–150 cases per year and 22 centers (3.6 %) even more than 151 cases per year.

Surgical management of EC

The extension, anatomic limit and indication for LND were the main surgical issues addressed. Whilst 330 (53.7 %) centers reported regularly performing LND, 43.4 % stated that LND was performed only in selected cases. Of those who performed LND, 66 % ($n = 408$) perform a systematic excision of nodes. Only 4 % of respondents undertook sampling of lymph nodes. The anatomic regions of LND included both pelvic and paraaortic resections ($n = 456$; 73.7 %), with 15 % limiting the lymphadenectomy to the pelvic nodes. The upper limit of paraaortic LND was different across all participants with 7.9 % setting the upper limit at the level of the inferior mesenteric artery (IMA), 75.5 % at the level of the renal veins and 2.9 % who stated that they routinely dissect the LN in the suprarenal area. There were statistically significant variations found between the different geographic regions not only regarding the type and extension of LND, but also the indication and intention of LND. The Asian countries (72.8 %) and CE-countries (55.6 %) routinely perform LND; countries in NE and SE as well as UK/USA/Canada routinely perform a LND in less than 1/3 of primary EC cases across all stages ($p < 0.001$). When questioned as to whether sampling or systematic LND are conducted, and whether the primary intent is treatment or staging, most centers from Asia (70.9 %) and CE (91 %) most commonly performed both pelvic and paraaortic systematic LND up to the level of the renal veins with the intention as both a therapeutic and staging procedure. Details are presented in detail in Tables 1 and 2.

The number of harvested lymph nodes (LN) characterized as adequate also strongly varied between the different geographic groups: 25.6 % of the Asian centers stated 21 LN as an adequate number of harvested paraaortic nodes, only 0–3.4 % of the other centers shared the same opinion ($p < 0.001$). Details are presented in Table 3 and in supplement [34] (Appendix S1).

Regarding the indications for LND, the following risk factors were cited: high grade histology: 553 (94.7 %); serous-papillary or clear-cell or adenosquamous histology: 531 (90.9 %); lymphovascular space invasion (L1): 378 (64.7 %); vascular space invasion (V1): 312 (53.4 %) and tumor diameter >2 cm: 276 (47.3 %). One-third of the participants (191; 32.3 %) reported performing a systematic LND only in stages I or II but not in more advanced stages, even in the presence of bulky pelvic or paraaortic LN. Centers from Asia

and CE were more likely to perform LND in well differentiated tumors, a large tumor diameter and lymphovascular space invasion compared to centers in SE, NE and USA/UK/Canada and Australia ($p < 0.001$). There was some concordance with respect to performing a systematic LND in the presence serous-papillary or clear cell histologies, with 90.5 % of all centers in agreement. Details are presented in Table 3.

The number of treated cases annually per center positively correlated with the stated ideal number of harvested pelvic and paraaortic LN. Data are presented in the supplemental section [34] (Appendix S1).

Adjuvant treatment of EC

In patients with stage pT1 or 2 disease and positive pelvic or paraaortic LN status (N1) the following treatment modalities were indicated (multiple options possible): vaginal brachytherapy 377(61 %); external beam radiation 329(53.2 %); chemotherapy alone 212(34.3 %); chemoradiotherapy 144(23.3 %); or no further treatment 45(7.5 %). Again, the responses varied significantly between different geographic regions. In the UK/USA/Canada centers, 84.1 % indicated a preference for vaginal brachytherapy and 70.5 % for external beam radiation, compared with only 5.6 % and 11.2 %, respectively, of Asian centers ($p < 0.001$). Asian centers indicated a strong preference for systemic chemotherapy 84.8 % against only 13.6 % of the UK/USA/Canada centers and 15.4 % of the Australia/New Zealand centers ($p < 0.001$). Detailed data are presented in Table 4. Accordingly, in stages pT3 and pT4, N1 disease, Asian centers continued to prefer systemic chemotherapy alone (93.6 %) as opposed to the majority of the UK/USA/Canada. NE and SE centers indicated combination chemo-radiotherapy as their treatment of choice (90.9, 77.8 and 80.8 %, respectively; $p < 0.001$) (Table 5).

In bivariate analysis, high-volume centers appeared to more frequently select vaginal brachytherapy over external beam radiotherapy ($p = 0.005$) and more frequently select systemic chemotherapy ($p < 0.001$) across all stages compared to low-volume centers. Moreover, 18 % of the high-volume centers did not employ any adjuvant treatment in completely staged serous-papillary EC compared to only 0.5 % of the low-volume centers ($p = 0.004$). Data are presented in supplement [34] (Appendix S1).

The most common chemotherapeutic regimes employed were: paclitaxel and carboplatin: 429 (69.4 %); doxorubicin and cisplatin: 133(21.5 %); doxorubicin and cisplatin and paclitaxel and G-CSF: 28(4.5 %) and single agent platinum: 18(2.9 %). Higher-volume centers tended to favor carboplatin and paclitaxel compared to low-volume centers ($p = 0.002$). Data are presented in Table 6.

Evaluating the impact of academic versus community center status, academic centers were significantly more likely to endorse treatment within the context of clinical trials ($p < 0.001$) and also to more frequently select chemotherapy alone over external beam radiation (81.1 % academic vs 54 % non-academic; $p < 0.001$). Data are presented in the supplemental section [34] (Appendix S1).

Discussion

This study is the largest international survey regarding the management of EC. It demonstrates significant differences between the various geographic areas in all levels of care—surgery, chemotherapy and irradiation. While centers from Asia together with centers from Central Europe were similar in terms of higher surgical radicality and preference for systemic chemotherapy over radiotherapy, centers from Northern and Southern Europe showed congruence to centers from USA/UK and Canada—manifest as a tendency towards a more conservative surgical approach with greater application of combination chemoradiotherapy rather than chemotherapy alone. Interestingly, high-volume centers did not necessarily predict greater use of treatment with the more modern therapeutics or greater surgical radicality; however, academic versus non-academic center status strongly predicted support and conduct of international and national trials.

This is a survey with all the hereby associated limitations and bias including the fact that the participants of the survey belonged to an anyway academically interested population that would encourage the actual participation in clinical trials, and hence there is the danger that our results would not represent the broad opinion of each country. A further significant limitation is that we do not have an overview of the subspecialty of the physicians from each center who participated and we cannot differentiate therefore between gynecological, medical or clinical oncologists. Also many countries are represented by only a very few number of participants and hence not ideally represented.

Contemporary treatment of EC-cancer patients depends tremendously on the country and center where the patients receive treatment; furthermore, individual physician preferences further contribute to the lack of consistency in EC treatment [5–9]. It is generally agreed that one of the most controversial topics in the management of EC is the value and the surgical extent of pelvic and paraaortic LND [10]. There is a complete lack of standardization regarding not just the surgical technique, but also the primary purpose of the procedure and indeed in which cases LND needs to be performed at all [11]. It would seem that the decision to perform systematic pelvic and/or paraaortic lymphadenectomy reflects the individual surgeon's preferences based on their personal experience and surgical expertise, patient comorbidity profile including body mass index, and age. Opponents of systematic LND cite the lack of any prospective evidence demonstrating a positive impact of LND on survival, while being associated with a more complex surgical procedure with added morbidity, longer operating times, higher blood loss and the risk of lymphedema and secondary cellulitis, especially when radiotherapy follows. Advocates of systematic pelvic and paraaortic LND, point out the flawed trial design that challenged the value of LND, where inadequate LND confined to the pelvis only or below the IMA was compared to complete omission of LND and hence—as expected, failing to show any survival benefit [5, 11–14, 31]. Through numerous mapping studies, it has been demonstrated that if EC has extended to a paraaortic node, the majority of metastases are in the area between the renal veins and IMA [3, 4, 15, 16]. Therefore a LND limited to the area below the IMA or just the pelvis will fail to show any kind of therapeutic benefit for staging with LND. Nevertheless, defining the value of systematic LND in EC will always be challenged by the level of surgical quality and skills required for dissection in the high paraaortic area, an obstacle that

is widely prevalent in multicentre international surgical trials where the surgical requirements are often lowered to facilitate inclusiveness of investigators and enhance enrolment [17, 32]. Two planned prospectively randomized trials initiated by the GOG and the AGO with parallel recruitment will attempt to definitively answer this unresolved issue of the role and extent of pelvic and paraaortic LND in EC. An also upcoming NCRI trial will attempt the same; however, the required extent of LND will be mandatory to the level of the IMA, though resection to the renal vessels can be performed.

One of the major challenges that obscure interpretation of current chemotherapy and radiotherapy trials are the broad differences in the baseline characteristics of the patients enrolled in terms of surgical treatment. The two large multicenter randomized PORTEC trials have established the value of vaginal brachytherapy in high-risk EC in terms of lower locoregional recurrence, but this trial failed to demonstrate any value of external beam radiotherapy in improving overall survival or lowering the risk distant metastases while negatively impacting overall quality of life in terms of clinically significant higher levels of bowel symptoms, limitations in daily activities and lower social functioning [18–25]. Interestingly, even though vaginal brachytherapy appeared to provide a better health related quality control, sexual symptoms were equally high in both cohorts [25]. A recently presented long-term follow-up of a previously published randomized study [26] on 568 EC-patients treated with external beam radiation between 1968 and 1974, showed that women younger than 60 years had a significantly poorer survival after external radiation with a significantly higher risk of secondary pelvic cancers [27]. Nevertheless, a great deal of diversity exists for the adjuvant treatment of high-risk stage-I and II EC with external beam radiotherapy vs. vaginal brachytherapy vs. even observation alone all being utilized depending on the physician's experience and preferences, country and center of treatment, degree of surgical radicality, and extent of lymph node resection. From this study, a clear distinguishable trend is observed whereby more conservative centers with regard to lymph node resection tended to more often utilize adjuvant radiotherapy, as opposed to centers that favored use of pelvic and paraaortic LND followed by either observation or systemic chemotherapy combined with vaginal brachytherapy. A currently recruiting large-scale randomized phase-III-trial of the American GOG is studying pelvic radiation therapy to evaluate its impact on PFS and OS compared with vaginal cuff brachytherapy followed by paclitaxel, and carboplatin in patients with high-risk stage-I or stage-II EC (NCT00807768). Equally inhomogeneous results were demonstrated in the actual choice of the chemotherapy agent. Some current national guidelines define doxorubicin and cisplatin as the evidence-based 1st-line treatment for EC, while other guidelines prefer carboplatin and paclitaxel due to the more favorable toxicity profile and observed phase-II-trial efficacy.

Conclusion

In conclusion, this study clearly demonstrated a lack of international consensus for primary and relapsed treatment of EC. The international community should therefore participate in the endeavor to find the optimum therapies through properly controlled trials, with respect to both survival and toxicity profile—it is what patients would expect. The fact that most centers expressed their willingness to participate in clinical trials provides hope that future

international collaboration with formation of a clinical trials network will provide definitive answers for the women afflicted with this disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Type and intention of lymph node dissection

Region	Do you perform lymphadenectomy in patients with endometrial cancer? $p < 0.001$			
	Never	In selected cases	Regularly/routinely	
Japan, Korea, Taiwan	N (%) 0	34 (27.2 %)	91 (72.8 %)	
Germany, Austria, Switzerland	N (%) 16 (4.4 %)	146 (40 %)	203 (55.6 %)	
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	N (%) 1 (5.6 %)	13 (72.2 %)	4 (22.2 %)	
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	N (%) 0	37 (72.5 %)	14 (27.5 %)	
Australia, New Zealand	N (%) 0	10 (76.9 %)	3 (23.1 %)	
United states, United Kingdom, Canada	N (%) 1 (2.3 %)	27 (62.8 %)	15 (34.9 %)	
Total	N (%) 18 (2.9 %)	267 (43.2 %)	330 (53.4 %)	

Region	Type of lymph node dissection $p < 0.001$			Intention of lymph node dissection $p < 0.001$	
	Sampling	Systematic	Both	Only staging	Therapeutic and staging
Japan, Korea, Taiwan	N (%) 3 (10.3 %)	23 (79.3 %)	3 (10.3 %)	37 (29.6 %)	84 (67.2 %)
Germany, Austria, Switzerland	N (%) 10 (3 %)	323 (96.7 %)	1 (0.3 %)	72 (20.7 %)	259 (74.6 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	N (%) 2 (16.7 %)	10 (83.3 %)	0	9 (50 %)	9 (50 %)
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	N (%) 4 (11.8 %)	30 (88.2 %)	0	26 (50 %)	24 (46.2 %)
Australia, New Zealand	N (%) 1 (10 %)	9 (90 %)	0	5 (38.5 %)	8 (61.5 %)
United states, United Kingdom, Canada	N (%) 5 (22.7 %)	13 (59.1 %)	4 (18.2 %)	23 (53.5 %)	20 (46.5 %)
Total	N (%) 25 (4 %)	408 (66 %)	8 (1.3 %)	172 (27.8 %)	404 (65.3 %)

Table 2

Extension and indications of lymphadenectomy among the different geographic regions

Region	Extension of lymph node dissection $p < 0.001$		Proximal anatomic limit of lymph node dissection $p < 0.001$			
	Only pelvic	Pelvic and paraaortic	Iliac communis artery	Inferior mesenteric artery	Renal vein	
Japan, Korea, Taiwan	N (%) 32 (29.1 %)	78 (70.9 %)	13 (10.4 %)	6 (4.8 %)	101 (80.8 %)	
Germany, Austria, Switzerland	N (%) 31 (9 %)	313 (91 %)	18 (5.2 %)	22 (6.3 %)	302 (86.5)	
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	N (%) 7 (53.8 %)	6 (46.2 %)	2 (11.8 %)	1 (5.9 %)	14 (82.4 %)	
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	N (%) 9 (23.1 %)	30 (76.9 %)	14 (27.5 %)	7 (13.7 %)	23 (45.1 %)	
Australia, New Zealand	N (%) 3 (37.5 %)	5 (62.5 %)	3 (23.1 %)	5 (38.5 %)	5 (38.5 %)	
United states, United Kingdom, Canada	N (%) 11 (31.4 %)	24 (68.6 %)	13 (30.2 %)	8 (18.6 %)	22 (51.2 %)	
Total	N (%) 93 (15.0 %)	456 (73.7 %)	63 (10.2 %)	49 (7.9 %)	467 (75.5 %)	

Region	When do you perform paraortic lymphadenectomy? $p < 0.001$			
	If indicated: always pelvic and paraaortic LND	Only if pelvic lymph nodes are affected (based on intraoperative frozen section)	Only if pelvic lymph nodes are affected (based on clinically suspected nodes)	
Japan, Korea, Taiwan	N (%) 63 (50.4 %)	9 (7.2 %)	53 (42.4 %)	
Germany, Austria, Switzerland	N (%) 260 (78.8 %)	70 (21.2 %)	0	
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	N (%) 8 (47.1 %)	6 (35.3 %)	3 (17.6 %)	
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	N (%) 28 (57.1 %)	13 (26.5 %)	8 (16.3 %)	
Australia, New Zealand	N (%) 5 (38.5 %)	5 (38.5 %)	3 (23.1 %)	
United states, United Kingdom, Canada	N (%) 20 (46.5 %)	4 (9.3 %)	19 (44.2 %)	
Total	n 384 (62.1 %)	107 (17.3 %)	86 (13.9)	

Table 3

By which additional risk factors do you indicate a lymph node dissection (multiple answers possible) and what is the adequate number of harvested lymph nodes?

Region	G3 ($p = 0.01$)	Tumor diameter >2 cm ($p < 0.001$)	Lymph angio space invasion (L1) ($p < 0.001$)	Haemangio space invasion (V1) ($p < 0.001$)	Serous-papillary or clear cell histology ($p = 0.725$)
Japan, Korea, Taiwan	120 (96 %)	46 (36.8 %)	78 (62.4 %)	64 (51.2 %)	110 (88 %)
Germany, Austria, Switzerland	321 (95.5 %)	185 (55.1 %)	245 (72.9 %)	205 (61 %)	307 (91.4 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	17 (94.4 %)	7 (38.9 %)	2 (11.1 %)	2 (11.1 %)	16 (88.9 %)
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	48 (92.3 %)	18 (34.6 %)	25 (48.1 %)	21 (40.4 %)	47 (90.4 %)
Australia, New Zealand	13 (100 %)	9 (62.9 %)	5 (38.5 %)	3 (23.1 %)	13 (100 %)
United states, United Kingdom, Canada	34 (79.1 %)	11 (25.6 %)	23 (53.3 %)	17 (39.5 %)	38 (88.4 %)
Total	553 (89.4 %)	276 (44.6 %)	378 (61.1 %)	312 (50.4 %)	531 (85.9 %)

Adequate number of harvested lymph nodes (per pelvic side)

Region	10 or less	11–15	16–20	21 or more
Japan, Korea, Taiwan	N (%) 1 (0.8 %)	14 (11.2 %)	36 (28.8 %)	74 (59.2 %)
Germany, Austria, Switzerland	N (%) 136 (39.3 %)	153 (44.2 %)	36 (10.4 %)	21 (6.1 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	N (%) 0	8 (44.4 %)	8 (44.4 %)	2 (11.1 %)
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	N (%) 3 (5.8 %)	26 (50 %)	16 (30.8 %)	7 (13.5 %)
Australia, New Zealand	N (%) 0	7 (53.8 %)	3 (23.1 %)	3 (23.1 %)
United states, United Kingdom, Canada	N (%) 3 (7.1 %)	24 (57.1 %)	12 (28.6 %)	3 (7.1 %)
Total	N (%) 143 (23.1 %)	232 (37.5 %)	111 (17.9 %)	110 (17.8 %)

What kind of adjuvant treatment do you recommend in FIGO stage I or II disease with positive lymph nodes (multiple answers possible)?

Table 4

Region	Vaginal brachytherapy ($p < 0.001$)	Pelvic external beam radiation ($p < 0.001$)	Chemotherapy ($p < 0.001$)	Radiochemo- therapy ($p < 0.001$)	No treatment ($p < 0.001$)
Japan, Korea, Taiwan	7 (5.6 %)	14 (11.2 %)	106 (84.8 %)	13 (10.4 %)	13 (10.4 %)
Germany, Austria, Switzerland	272 (78.8 %)	235 (68.1 %)	73 (21.2 %)	91 (26.4 %)	8 (2.2 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	10 (55.6 %)	8 (44.4 %)	3 (16.7 %)	4 (22.2 %)	7 (38.9 %)
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	41 (78.8 %)	37 (71.2 %)	22 (42.3 %)	21 (40.4 %)	6 (11.5 %)
Australia, New Zealand	10 (76.9 %)	4 (30.8 %)	2 (15.4 %)	3 (23.1 %)	4 (30.8 %)
United states, United Kingdom, Canada	37 (84.1 %)	31 (70.5 %)	6 (13.6 %)	12 (27.3 %)	7 (15.9 %)
Total	377 (61 %)	329 (53.2 %)	212 (34.3 %)	144 (23.3 %)	45 (7.3 %)

What kind of adjuvant treatment do you recommend in FIGO stage III or IV disease with positive lymph nodes (multiple answers possible)?

Table 5

Region	Vaginal brachytherapy ($p < 0.001$)	Pelvic external beam radiation ($p < 0.001$)	Paraaortic external beam radiation ($p < 0.001$)	Chemotherapy ($p < 0.001$)	Radiochemo- therapy ($p < 0.001$)	No treatment ($p < 0.001$) ($p = 0.436$)
Japan, Korea, Taiwan	2 (1.6 %)	5 (4 %)	3 (2.4 %)	117 (93.6 %)	38 (30.4 %)	1 (0.8 %)
Germany, Austria, Switzerland	187 (54.4 %)	154 (44.8 %)	134 (39 %)	163 (47.4 %)	162 (47.1 %)	3 (0.8 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	4 (22.2 %)	5 (27.8 %)	4 (22.2 %)	14 (77.8 %)	14 (77.8 %)	0
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	15 (28.8 %)	16 (30.8 %)	6 (11.5 %)	41 (78.8 %)	42 (80.8 %)	0
Australia, New Zealand	2 (15.4 %)	4 (30.8 %)	2 (15.4 %)	7 (53.8 %)	8 (61.5 %)	0
United states, United Kingdom, Canada	16 (36.4 %)	12 (27.3 %)	10 (22.7 %)	35 (79.5 %)	40 (90.9 %)	2 (4.5 %)
Total	226 (36.5 %)	196 (31.7 %)	159 (25.7 %)	377 (61 %)	304 (49 %)	6 (1 %)

When you indicate chemotherapy alone for EC which treatment regime do you mostly apply?

Table 6

Region	Carboplatin + Paclitaxel ($p < 0.001$)	Doxorubicin + Cisplatin ($p < 0.001$)	Doxorubicin + Cisplatin + Paclitaxel + G-CSF ($p < 0.001$)	Platinum Monotherapy ($p = 0.038$)	Other ($p = 0.13$)
Japan, Korea, Taiwan	99 (79.2 %)	21 (16.8 %)	1 (0.8 %)	0	4 (3.2 %)
Germany, Austria, Switzerland	223 (69.7 %)	106 (33.1 %)	19 (5.9 %)	17 (5.3 %)	6 (1.9 %)
Belgium, Denmark, Finland, Norway, Sweden, Netherlands	17 (94.4 %)	1 (5.6 %)	0	0	0
Portugal, Spain, Greece, Italy, Poland, Israel, Turkey	35 (67.3 %)	5 (9.6 %)	8 (15.4 %)	0	5 (9.6 %)
Australia, New Zealand	13 (100 %)	0	0	0	0
United states, United Kingdom, Canada	42 (95.5 %)	0	0	1 (2.3 %)	1 (2.3 %)
Total	429 (69.4 %)	133 (21.5 %)	28 (4.5 %)	18 (2.9 %)	16 (2.6 %)